25. (New) An isolated nucleic acid comprising a nucleic acid sequence which encodes a domain of a ramoplanin nonribosomal peptide synthetase, wherein said ramoplanin nonribosomal peptide synthetase comprises an amino acid sequence of SEQ ID NO: 13, SEQ ID NO: 14, SEQ ID NO: 15 or SEQ ID NO: 18.

26. (New) The isolated nucleic acid of claim 25, wherein said domain is a condensation domain, an adenylation domain, a thiolation domain or a thioesterase domain.

27. (New) The isolated nucleic acid of claim 25 wherein said ramoplanin nonribosomal peptide synthetase comprises an amino acid sequence of SEQ ID NO: 13.

28. (New) The isolated nucleic acid of claim 25 wherein said ramoplanin nonribosomal peptide synthetase comprises an amino acid sequence of SEQ ID NO: 14.

29. (New) The isolated nucleic acid of claim 25 wherein said ramoplanin nonribosomal peptide synthetase comprises an amino acid sequence of SEQ ID NO: 15.

30. (New) The isolated nucleic acid of claim 25 wherein said ramoplanin nonribosomal peptide synthetase comprises an amino acid sequence of SEQ ID NO: 18.

31. (New) The isolated nucleic acid of claim 26, wherein said condensation domain comprises an amino acid sequence selected from the group consisting of: amino acids 1-470 of SEQ ID NO: 13; amino acids 1-517 of SEQ ID NO: 14, amino

acids 1106-1560 of SEQ ID NO: 14; amino acids 2159-2618 of SEQ ID NO: 14; amino acids 3237-3697 of SEQ ID NO: 14; amino acids 4241-4718 of SEQ ID NO: 14; amino acids 5307-5754 of SEQ ID NO: 14; amino acids 5838-6317 of SEQ ID NO: 14; amino acids 1-470 of SEQ ID NO: 15; amino acids 1109-1567 of SEQ ID NO: 15; amino acids 2122-2602 of SEQ ID NO: 15; amino acids 3212-3671 of SEQ ID NO: 15; amino acids 4217-4698 of SEQ ID NO: 15; amino acids 5317-5776 of SEQ ID NO: 15; amino acids 6363-6839 of SEQ ID NO: 15 and amino acids 7458-7925 of SEQ ID NO: 15.

32. (New) The isolated nucleic acid of claim 26, wherein said adenylation domain comprises an amino acid sequence selected from the group consisting of: amino acids 471-959 of SEQ ID NO: 13; amino acids 518-990 of SEQ ID NO: 14; amino acids 1561-2052 of SEQ ID NO. 14; amino acids 2619-3122 of SEQ ID NO: 14; amino acids 3698-4160 of SEQ ID NO: 14; amino acids 4179-5192 of SEQ ID NO: 14; amino acids 6318-6804 of SEQ ID NO: 14; amino acids 487-993 of SEQ ID NO: 15; amino acids 1568-2041 of SEQ ID NO: 15; amino acids 2603-3095 of SEQ ID NO: 15; amino acids 3672-4135 of SEQ ID NO: 15; amino acids 4699-5199 of SEQ ID NO: 15; amino acids 5777-6280 of SEQ ID NO: 15; amino acids 6840-7343 of SEQ ID NO: 15 and amino acids 7296-8380 of SEQ ID NO: 15.

33. (New) The isolated nucleic acid of claim 26, wherein said thiolation domain comprises an amino acid sequence selected from the group consisting of amino acids 961-1030 of SEQ ID NO: 13; amino acids 991-1059 of SEQ ID NO: 14; amino acids 2054-2122 of SEQ ID NO: 14; amino acids 3123-3191 of SEQ ID NO: 14; amino acids 4161-4228 of SEQ ID NO: 14; amino acids 5193-5260 of SEQ ID NO: 14; amino acids 5755-5824 of SEQ ID NO: 14; amino acids 6805-6873 of SEQ ID NO 14; amino acids 994-1062 of SEQ ID NO: 15; amino acids 2042-2110 of SEQ ID NO: 15; amino acids 3097-3165 of SEQ ID NO: 15;

amino acids 4136-4202 of SEQ ID NO: 15; amino acids 5200-5268 of SEQ ID NO: 15; amino acids 6281-6350 of SEQ ID NO: 15; amino acids 7344-7411 of SEQ ID NO: 15 and amino acids 8381-8449 of SEQ ID NO: 15.

34. (New) The isolated nucleic acid of claim 26, wherein said thioesterase domain comprises an amino acid sequence of amino acids 8450-8695 of SEQ ID NO. 15.

35. (New) The isolated nucleic acid of claim 27, wherein said nucleic acid sequence encodes an amino acid sequence selected from the group consisting of : amino acids 1-470 of SEQ ID NO. 13, amino acids 471-959 of SEQ ID NO. 13 and amino acids 961-1030 of SEQ ID NO. 13.

36. (New) The isolated nucleic acid of claim 28, wherein said nucleic acid sequence encodes an amino acid sequence selected from the group consisting of: amino acids 1-517 of SEQ ID NO: 14; amino acids 518-990 of SEQ ID NO: 14; amino acids 991-1059 of SEQ ID NO: 14; amino acids 1106-1560 of SEQ ID NO: 14; amino acids 1561-2052 of SEQ ID NO: 14; amino acids 2054-2122 of SEQ ID NO: 14; amino acids 2159-2618 of SEQ ID NO: 14; amino acids 2619-3122 of SEQ ID NO: 14; amino acids 3123-3191 of SEQ ID NO: 14; amino acids 3237-3697 of SEQ ID NO: 14; amino acids 3698-4160 of SEQ ID NO: 14; amino acids 4161-4228 of SEQ ID NO: 14; amino acids 4241-4718 of SEQ ID NO: 14; amino acids 4719-5192 of SEQ ID NO: 14; amino acids 5193-5260 of SEQ ID NO: 14; amino acids 5307-5754 of SEQ ID NO: 14; amino acids 5755-5824 of SEQ ID NO: 14; amino acids 5838-6317 of SEQ ID NO: 14; amino acids 6318-6804 of SEQ ID NO: 14 and amino acids 6805-6873 of SEQ ID NO: 14.

37. (New) The isolated nucleic acid of claim 29, wherein said nucleic acid sequence encodes an amino acid sequence selected from the group consisting of: amino acids 1-486 of SEQ ID NO: 15; amino acids 487-993 of SEQ ID NO: 15; amino

acids 994-1062 of SEQ ID NO: 15; amino acids 1109-1567 of SEQ ID NO: 15; amino acids 1568-2041 of SEQ ID NO: 15; amino acids 2042-2110 of SEQ ID NO: 15; amino acids 2122-2602 of SEQ ID NO: 15; amino acids 2603-3095 of SEQ ID NO: 15; amino acids 3097-3165 of SEQ ID NO: 15; amino acids 3212-3671 of SEQ ID NO: 15; amino acids 3672-4135 of SEQ ID NO: 15; amino acids 4136-4202 of SEQ ID NO: 15; amino acids 4217-4698 of SEQ ID NO: 15; amino acids 4699-5199 of SEQ ID NO: 15; amino acids 5200-5268 of SEQ ID NO: 15; amino acids 5317-5776 of SEQ ID NO: 15; amino acids 5777-6280 of SEQ ID NO: 15; amino acids 6281-6350 of SEQ ID NO: 15; amino acids 6363-6839 of SEQ ID NO: 15; amino acids 6840-7343 of SEQ ID NO: 15; amino acids 7344-7411 of SEQ ID NO: 15; amino acids 7458-7925 of SEQ ID NO: 15; amino acids 7926-8380 of SEQ ID NO: 15; amino acids 8381-8449 of SEQ ID NO: 15; and amino acids 8450-8695 of SEQ ID NO: 15.

38. (New) The isolated nucleic acid of claim 27, wherein said nucleic acid comprises a coding sequence identical to or complementary to nucleotides 15880-19035 of SEQ ID NO: 1 or a sequence that encodes an amino acid sequence of SEQ ID NO: 13.

39. (New) The isolated nucleic acid of claim 28, wherein said nucleic acid comprises a coding sequence identical to or complementary to nucleotides 19032-39713 of SEQ ID NO: 1 or a sequence that encodes an amino acid sequence of SEQ ID NO: 14.

40. (New) The isolated nucleic acid of claim 29, wherein said nucleic acid comprises a coding sequence identical to or complementary to nucleotides 39713-65800 of SEQ ID NO: 1 or a sequence that encodes an amino acid sequence of SEQ ID NO: 15.

41. (New) The isolated nucleic acid of claim 30, wherein said nucleic acid comprises a coding sequence identical to or complementary to nucleotides 67384-70059 of SEQ ID NO: 1 or a sequence that encodes an amino acid sequence of SEQ ID NO: 18.

42. (New) The isolated nucleic acid of claim 1, wherein said nucleic acid is identical to or complementary to SEQ ID NO: 1.

43. (New) An expression vector comprising a nucleic acid of claim 25.

44. (New) A host cell transformed with an expression vector of claim 43.

45. (New) A method of preparing ramoplanin or an analog thereof, comprising transforming a host cell with an expression vector of claim 43, culturing said host cell under conditions such that a ramoplanin synthase is produced and catalyzes the synthesis of said ramoplanin or analog thereof.

In the Specification:

Please replace the paragraph beginning at page 1, line 3, with the following replacement paragraph:

--This application claims benefit under 35 USC §119 of provisional application USSN 60/239,924 filed on October 13, 2000 and of provisional application USSN 60/283,296 filed April 12, 2001, and claims benefit under 35 USC §120 of USSN 09/910,813 which are hereby incorporated by reference in their entirety for all purposes--

Please replace the paragraph beginning at page 3, line 6 with the following replacement paragraph:

-- The present invention provides purified and isolated polynucleotide molecules that encode polypeptides of the ramoplanin biosynthetic pathway in microorganisms. In one form of the invention, polynucleotide molecules are selected from the contiguous DNA sequence (SEQ ID NO: 1) representing the full-length locus of the ramoplanin biosynthetic pathway and containing the 33 ORFs encoding the proteins forming the ramoplanin gene cluster. The amino acid sequence of the proteins is provided in SEQ ID NOS: 2 to 34. Structural and functional characterization is provided for the 33 ORFs.--

Please replace the paragraph beginning at page 3, line 21 with the following replacement paragraph:

--Certain embodiments of the invention specifically exclude one or more of ORFs 1 to 33, most notably ORFs 1, 2, 3, 6, 7, 8, 20, 21, 27, 28, 31 and 32 (SEQ ID NOS: 2, 3, 4, 7, 8, 9, 21, 22, 28, 29, 32 and 33) although other ORFs can be excluded without departing from the scope of the invention. Thus, another embodiment of the invention provides an isolated nucleic acid comprising a nucleic acid sequence selected from the group consisting of: (a) a nucleic acid encoding any of ramoplanin ORFs 4, 5, 9 to 19, 22 to 26, 29, 30 and 31 (SEQ ID NOS: 5, 6, 10 to 20, 23 to 27, 30, 31 and 32); (b) a nucleic acid encoding a polypeptide encoded by any of ramoplanin ORFs 4, 5, 9 to 19, 22 to 26, 29, 30 and 31 (SEQ ID NOS: 5, 6, 10 to 20, 23 to 27, 30, 31 and 32); and (c) a nucleic acid encoding a polypeptide that is at least 75%, preferably 80%, more preferably 85%, still more preferably 90% and most preferably 95% or more identical in amino acid sequence to a polypeptide of ramoplanin ORFs 4, 5, 9 to 19, 22 to 26, 29, 30 and 31 (SEQ ID NOS: 5, 6, 10 to 20, 23 to 27, 30, 31 and 32).--

Please replace the paragraph beginning at page 4, line 1, with the following replacement paragraph:

--In one embodiment preferred nucleic acids encode at least two, more preferably three, still more preferably four, or most preferably or more ORFs selected from ORFS 1 to 33 (SEQ ID NOS: 2 to 34) of the ramoplanin locus. In one embodiment, combinations of ORFs selected from ORFs 1 through 33 (SEQ ID NOS 2 to 34) are provided which encode polypeptides that form at least the depsipeptide core structure of ramoplanin. In another embodiment combinations of ORFs selected from ORFs 1 through 33 (SEQ ID NOS: 2 to 34) are provided which encode polypeptides that form at least the fatty-aid side chain of the depsipeptide core structure of ramoplanin. In another embodiment, combinations of ORFs selected from ORFs 1 through 33 (SEQ ID NOS: 2 to 34) are provided which encode polypeptides responsible for the synthesis of 4-hydroxyphenylglycine (HPG) of ramoplanin. In another embodiment, combinations of ORFs selected from ORFs 1 through 33 (SEQ ID NOS: 2 to 34) are provided that encode polypeptides that form at least the beta-hydroxyasparagine residue. In another embodiment, combinations of ORFs selected from ORFs 1 through 33 (SEQ ID NOS: 2 to 34) are provided which are involved in the regulation of ramoplanin biosynthesis. In another embodiment, combinations of ORFs selected from ORFs 1 through 33 (SEQ ID NOS: 2 to 34) are provided which encode polypeptides that are involved in resistance and subcellular localization of the ramoplanin biosynthetic machinery. A single ORF or a combination of ORFs selected from ORFs 1 through 33 (SEQ ID NOS: 2 to 34) are provided to enhance production of ramoplanin by altering the expression level of an ORF selected from ORFs 1 through 33 (SEQ ID NOS: 2 to 34). In another embodiment, the expression level of an ORF selected from ORFs 1 through 33 (SEQ ID NOS: 2 to 34) may be altered to increase the yield of a particular form of ramoplanin.--

Please replace the paragraph beginning at page 10, line 30 with the following replacement paragraph:

--Ramoplanins are naturally produced by the microorganism *Actinoplanes sp.* ATCC 33076. The genetic locus encoding the biosynthetic pathway for ramoplanin production

was isolated and cloned by the procedure described in USSN 09/910,813, from genomic DNA isolated from a ramoplanin producing strain of *Actinoplanes sp.* ATCC 33076 (obtained from the American Type Culture Collection, Manassas, VA, USA). This newly discovered locus encodes 33 individual proteins involved in the biosynthesis of ramoplanin by this organism. The 33 proteins are encoded by ORFs contained within the contiguous sequence of 88421 base pairs of DNA (SEQ ID NO: 1).--